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Randomized cross-over evaluation of body-surface area-based dosing versus flat-fixed dosing of paclitaxel.

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PURPOSE: Despite dose calculation using body-surface area (BSA), pharmacokinetics of most anticancer drugs show wide interindividual variability. In this study, we evaluated the role of BSA in paclitaxel disposition. PATIENTS AND METHODS: Paclitaxel pharmacokinetics were prospectively studied in 12 patients that were treated in a randomized cross-over design with paclitaxel (3-hour infusion at a 3-week interval) at 175 mg/m2 in cycle 1 (A) and a flat-fixed dose of 300 mg in cycle 2 (B), or vice versa. Blood samples were collected up to 24 hours after dosing and analyzed for total and unbound paclitaxel. RESULTS: The area under the curves (AUC) of unbound paclitaxel were similar in both dosing groups, with mean values +/- SD (A v B) of 1.34 +/- 0.158 versus 1.30 +/- 0.329 microM x h, indicating that BSA-based dosing reduced the coefficient of variation by 53.3%. Unbound and total paclitaxel clearance was also significantly related to various body-size measures, including BSA (R > or = 0.617; P < or =.033), weight (R >or = 0.621; P < or =.031), and lean-body mass (r > or = 0.630; P < or = .028). We hypothesize that this is caused by the association of paclitaxel in the circulation with Cremophor EL, the distribution of which is linked to total blood volume, and thus to BSA. CONCLUSION: This study indicates that paclitaxel disposition is significantly related to BSA. This provides a pharmacokinetic rationale for BSA-based dosing of this drug.

Publication Types:

- Clinical Trial
- Randomized Controlled Trial

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